

# PATENT COOPERATION TREATY

PCT/RS

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

<b>To:</b> <b>AVECIA LIMITED</b> Attn. Gairns, Raymond S. Intellectual Property Group P.O. Box 42, Hexagon House Blackley, Manchester M9 8ZS UNITED KINGDOM
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(PCT Rule 44.1)

<b>Applicant's or agent's file reference</b> SMC 60598/WO
<b>International application No.</b> PCT/GB2004/002478

<b>Date of mailing</b> (day/month/year)	16/02/2005
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<b>FOR FURTHER ACTION</b>	See paragraphs 1 and 4 below
<b>International filing date</b> (day/month/year)	09/06/2004

<b>Applicant</b> AVECIA LIMITED
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1. <input checked="" type="checkbox"/>	<p>The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.</p> <p><b>Filing of amendments and statement under Article 19:</b>          The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):</p> <p style="padding-left: 20px;">When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.</p> <p style="padding-left: 20px;">Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes          1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35</p> <p><b>For more detailed instructions, see the notes on the accompanying sheet.</b></p>
2. <input type="checkbox"/>	<p>The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.</p>
3. <input type="checkbox"/>	<p><b>With regard to the protest</b> against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that</p> <p><input type="checkbox"/> the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.</p> <p><input type="checkbox"/> no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.</p>
4. Reminders	<p><b>Shortly after the expiration of 18 months</b> from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.</p> <p>The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.</p> <p>Within <b>19 months</b> from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until <b>30 months</b> from the priority date (in some Offices even later); otherwise, the applicant must, within <b>20 months</b> from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.</p> <p>In respect of other designated Offices, the time limit of <b>30 months</b> (or later) will apply even if no demand is filed within 19 months.</p> <p>See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the <i>PCT Applicant's Guide</i>, Volume II, National Chapters and the WIPO Internet site.</p>

DATE ENTERED INTO SYSTEM  
 INDEXED  
 SERIALIZED  
 FILED  
 MAR 01 2005  
 PCT/RS

<b>Name and mailing address of the International Searching Authority</b> European Patent Office, P.B. 5618 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016
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<b>Authorized officer</b> Tanja Rührmund
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## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>SMC 60598/WO</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB2004/002478</b>	International filing date (day/month/year) <b>09/06/2004</b>	(Earliest) Priority Date (day/month/year) <b>13/06/2003</b>
Applicant <b>AVECIA LIMITED</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☒ Unity of invention is lacking (see Box III).

4. With regard to the title



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/GB2004/002478

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C209/14 C07C209/16 C07B57/00 C07C211/27 C07C309/66  
C07C29/143

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	W. H. PIRKLE ET AL.: "High pressure assisted synthesis." JOURNAL OF ORGANIC CHEMISTRY., vol. 42, no. 18, 1977, pages 3101-3103, XP002300103 USAMERICAN CHEMICAL SOCIETY, WASHINGTON, DC. page 3102, column 2 -----	1
Y	JAYARAM R. TAGAT ET AL.: "Piperazine-based CCR5 antagonists as HIV-1 inhibitors." JOURNAL OF MEDICINAL CHEMISTRY., vol. 44, no. 21, 2001, pages 3343-3346, XP002300104 USAMERICAN CHEMICAL SOCIETY. WASHINGTON. page 3344, scheme 2 ----- -/-	1-9, 11-16

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

Name and mailing address of the ISA  
European Patent Office, P.B. 5816 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax. (+31-70) 340-3016

Authorized officer

Rufet, J

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00/66558 A (MCCOMBIE STUART W ; SMITH ELIZABETH M (US); CLADER JOHN W (US); SCHERI) 9 November 2000 (2000-11-09) page 80 - page 81 -----	1-9, 11-16
Y	WO 98/42643 A (MELLOR BEN J ; ZENECA LTD (GB); BLACKER ANDREW J (GB)) 1 October 1998 (1998-10-01) cited in the application page 5, line 15 - line 17; claims 1-24; examples 1-19 -----	1-9, 11-16
Y	US 5 767 276 A (ZHANG XUMU) 16 June 1998 (1998-06-16) cited in the application claims 1-35; table I -----	1-9, 11-16
Y	WO 99/24410 A (UNIV PENNSYLVANIA) 20 May 1999 (1999-05-20) cited in the application claim 1; tables 1,2 -----	1-9, 11-16
Y	US 6 391 865 B1 (MCCOMBIE STUART W ET AL) 21 May 2002 (2002-05-21) page 9, scheme 2 -----	1-9, 11-16
Y	BJÖRN M. NILSSON ET AL.: "Base-Catalysed cyclization of N-propargylamides to Oxazoles" JOURNAL OF HETEROCYCLIC CHEMISTRY, vol. 26, 1989, pages 269-275, XP002300105 page 272, column 2 -----	1,11
Y	PATENT ABSTRACTS OF JAPAN vol. 2002, no. 02, 2 April 2002 (2002-04-02) & JP 2001 294568 A (CENTRAL GLASS CO LTD), 23 October 2001 (2001-10-23) abstract -----	1,11
Y	WO 86/01502 A (DIAMALT AG) 13 March 1986 (1986-03-13) example 2 -----	1
X	DATABASE CROSSFIRE BEILSTEIN BEILSTEIN INSTITUT ZUR FOERDERUNG DER CHEMISCHEN WISSENSCHAFTEN, FRANKFURT AM MAIN, DE; Database-Accession no. 4377580 (ID) XP002300107 abstract & JOURNAL OF ORGANIC CHEMISTRY., vol. 60, no. 26, 1995, pages 8424-8427, USAMERICAN CHEMICAL SOCIETY, WASHINGTON, DC. -----	21
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RANU B C ET AL: "Reduction of trihalomethyl carbinols and their acetates, mesylates and tosylates by indium metal" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 43, no. 34, 19 August 2002 (2002-08-19), pages 5993-5995, XP004373219 ISSN: 0040-4039 table 1 -----	21
X	THOMAS M. STEIN ET AL.: "Synthesis and aggregation properties of a new family of amphiphiles with an unusual headgroup topology" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 114, no. 10, 1992, pages 3943-3950, XP002300106 USAMERICAN CHEMICAL SOCIETY, WASHINGTON, DC. Scheme II; page 3948, column 2, paragraph 2 -----	21

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2004/002478

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-17, 21, 22

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17,21,22

Process for the preparation of an amine of formula (1) wherein an intermediate compound having a leaving group OL is reacting with ammonia and mesylate intermediates thereof  
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2. claim: 18

Alternative process for the preparation of a stereoisomer of an alcohol compound of formula (14)  
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3. claims: 19,20

Alternative process for the diastereomeric salt resolution of (S)-1-naphthylethylamine and diastereomeric salt thereof  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/002478

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0066558	A	09-11-2000	AU 4500900 A 17-11-2000
			BR 0010304 A 13-02-2002
			CA 2371583 A1 09-11-2000
			CZ 20013940 A3 17-04-2002
			EP 1175401 A1 30-01-2002
			HU 0202867 A2 28-01-2003
			JP 2002543185 T 17-12-2002
			NO 20015366 A 03-01-2002
			PL 351388 A1 07-04-2003
			SK 15692001 A3 02-07-2002
			TR 200103214 T2 21-03-2002
			WO 0066558 A1 09-11-2000
			US 6391865 B1 21-05-2002
			ZA 200108868 A 27-01-2003
WO 9842643	A	01-10-1998	AT 222223 T 15-08-2002
			AU 739341 B2 11-10-2001
			AU 6739198 A 20-10-1998
			CA 2284777 A1 01-10-1998
			CN 1130324 C 10-12-2003
			CZ 9903374 A3 15-12-1999
			DE 69807199 D1 19-09-2002
			DE 69807199 T2 08-05-2003
			DK 971865 T3 09-12-2002
			EP 0971865 A1 19-01-2000
			ES 2182288 T3 01-03-2003
			WO 9842643 A1 01-10-1998
			HU 0002058 A2 28-10-2000
			IL 131913 A 12-05-2004
			JP 2002501490 T 15-01-2002
			NO 994677 A 24-11-1999
			PT 971865 T 29-11-2002
			US 2002156282 A1 24-10-2002
			US 6372931 B1 16-04-2002
US 5767276	A	16-06-1998	AU 7446196 A 30-04-1997
			EP 0871621 A1 21-10-1998
			JP 11514356 T 07-12-1999
			WO 9713763 A1 17-04-1997
WO 9924410	A	20-05-1999	AU 1398199 A 31-05-1999
			BR 9814167 A 26-09-2000
			CA 2308415 A1 20-05-1999
			CN 1278801 T 03-01-2001
			EP 1030849 A1 30-08-2000
			HU 0100419 A2 28-05-2001
			JP 2001522838 T 20-11-2001
			PL 340767 A1 26-02-2001
			TR 200001333 T2 23-10-2000
			WO 9924410 A1 20-05-1999
			US 6255493 B1 03-07-2001
			US 2001044546 A1 22-11-2001
US 6391865	B1	21-05-2002	US 2003069252 A1 10-04-2003
			US 2004067961 A1 08-04-2004
			AU 4500900 A 17-11-2000
			BR 0010304 A 13-02-2002
			CA 2371583 A1 09-11-2000

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/002478

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6391865	B1	CZ 20013940 A3 EP 1175401 A1 HU 0202867 A2 JP 2002543185 T NO 20015366 A PL 351388 A1 SK 15692001 A3 TR 200103214 T2 WO 0066558 A1 ZA 200108868 A	17-04-2002 30-01-2002 28-01-2003 17-12-2002 03-01-2002 07-04-2003 02-07-2002 21-03-2002 09-11-2000 27-01-2003
JP 2001294568	A	23-10-2001	NONE
WO 8601502	A	13-03-1986	DE 3431591 A1 AT 57680 T DE 3580266 D1 WO 8601502 A1 EP 0190322 A1 JP 62501068 T
			13-03-1986 15-11-1990 29-11-1990 13-03-1986 13-08-1986 30-04-1987

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2004/002478

International filing date (day/month/year)  
09.06.2004

Priority date (day/month/year)  
13.06.2003

International Patent Classification (IPC) or both national classification and IPC  
C07C209/14, C07C209/16, C07B57/00, C07C211/27, C07C309/66, C07C29/143

Applicant  
AVECIA LIMITED

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



European Patent Office - Gitschiner Str. 103  
D-10958 Berlin  
Tel. +49 30 25901 - 0  
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Authorized Officer

Rufet, J

Telephone No. +49 30 25901-332



WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

**10/560305**  
International application No.  
PCT/GB2004/002478

**IAP20 Rec'd PCT/770 12 DEC 2005**

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/002478

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**Box No. II    Priority**

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1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
4. Additional observations, if necessary:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/002478

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 18-20

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 18-20
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- the written form ☐ has not been furnished
- ☐ does not comply with the standard
- the computer readable form ☐ has not been furnished
- ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/002478

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**Box No. IV Lack of unity of invention**

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1. ☒ In response to the invitation (Form PCT/SA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
  - ☐ paid additional fees under protest.
  - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-17,21,22

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**Box No. V Reasoned statement under Rule 43b/is.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	2-17,22
	No: Claims	1,21
Inventive step (IS)	Yes: Claims	10,17
	No: Claims	1-9,11-16
Industrial applicability (IA)	Yes: Claims	1-17,21,22
	No: Claims	

2. Citations and explanations

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

PCT/GB2004/002478

IAP20 Rec'd PCT/PTO 12 DEC 2005

**Re Item III.**

A non-unity objection has been raised during the search stage. The Applicant has not paid extra fees, therefore no search report has been issued for the subject-matter of the claims 18-20.

Consequently no opinion will be given for the subject-matter of these claims.

**Re Item IV.**

The ISA found multiple inventions in this application as follow:

**Invention I (claims 1-17,21,22)**

Process for the preparation of an amine of formula (1) wherein an intermediate compound having a leaving group OL is reacting with ammonia and mesylate intermediates thereof

**Invention II (claim 18)**

Alternative process for the preparation of a stereoisomer of an alcohol compound of formula (14)

**Invention III (claims 19,20)**

Alternative process for the diastereomeric salt resolution of (S)-1-naphthylethylamine and diastereomeric salt thereof

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The inventions listed above a priori do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature which defines the contribution of invention I over the prior art is, according to the applicant, the specific sequence of steps (a), (b) and (c). It is pointed out that compounds of formula (1) are well known compounds e.g. (S)-1-(1-naphthyl)ethylamine, RN: 10420-89-0).

The special technical feature of invention II is the step of reducing a ketone of formula (6) into the corresponding stereoisomer alcohol of formula (14); it is also stressed that compounds of formulae (14) and (6) are well known compounds, e.g. RN: 15914-84-8,



RN: 42177-25-3, RN: 941-98-0.

The special technical feature of invention III is to carry out the resolution of the known (S)-1-naphthylethylamine using tartaric acid or (S)-chloropropionic acid.

Moreover it is pointed out that according to the PCT Gazette-Section IV, (g)(v), a requirement for unity is that the intermediate and the final products shall not be separated, in the process leading from one to the other, by an intermediate which is not novel, which is not the case in the present application.

Due to the fact that no other technical features can be regarded as special technical feature in the sense of rule 13.2 PCT, the ISA is of the opinion that there is no single inventive concept underlying the 3 inventions in the sense of rule 13.1 PCT.

Since the Applicant did not paid additional search fees the examination has been limited to the first invention mentioned.

**Re Item V.**

1. The following documents are referred to in this communication:

- D1: J. ORG. CHEM., vol. 42, no. 18, 1977, pages 3101-3103, XP002300103
- D2: J. MED. CHEM., vol. 44, no. 21, 2001, pages 3343-3346, XP002300104
- D3: WO 00/66558 A
- D4: US 6 391 865 B1
- D5: WO 98/42643 A cited by Applicant
- D6: US 5 767 276 A cited by Applicant
- D7: WO 99/24410 A cited by Applicant
- D8: J. HETEROCYCLIC CHEM., vol. 26, 1989, pages 269-275, XP002300105
- D9: JP 2001 294568 A
- D10: WO 86/01502 A
- D11: DATABASE CROSSFIRE BEILSTEIN; Database-Accession no. 4377580 (ID) XP002300107
- D12: TETRAHEDRON LETTERS, vol. 43, no. 34, 2002, pages 5993-5995,
- D13: J.A.C.S., vol. 114, no. 10, 1992, pages 3943-3950, XP002300106

## **2. Novelty**

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT in view of the teaching of D1.

Document D1 discloses a process for the preparation of a primary amine (1-phenylethylamine derivative) falling under formula (1) of present claim 1 comprising the steps (a), (b) and © as claimed; see especially page 3102, column 2.

2.2 A process for the preparation of a 1-naphthylethylamine compound of formula (5) according to claims 2-17, comprising the steps (a), (b) and (c) is not described in the prior art documents D1-D10.

Documents D2-D4, D8-D10 refer to the preparation of 1-phenylethylamine derivatives instead of 1-naphthylethylamine derivatives (see D2, scheme 2; D3, p. 80-81; D4, p. 9, scheme 2; D8, scheme I; D9, abstract; D10, example 2)

Documents D5-D7 refer to the reducing step (a) as claimed.

2.3 Compound claims 21, 22

D11-13 disclose mesylate compounds falling under the scope of formula (15) of claim 21 and are therefore novelty destroying documents for claim 21.

the compound of formula (16) of claim 22 appears to be novel over the prior art.

## **3. Inventive step**

3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claims 2-9, 11-16 does not involve an inventive step in the sense of Article 33(3)PCT.

3.2 Documents D1-D4 are considered to represent equally the most relevant state of the art to the subject matter of claim 2, because each of these documents discloses an analogy process of the process of claim 2, which differs only by the nature of the starting compound i.e 1-phenylethylamine derivative instead of a 1-naphthylethylamine derivative.

3.3 The subject-matter of claim 2 differs from the disclosure of D5-D7 in that only the catalytic reduction of a naphthyl ketone of formula (6) (step (a)) as claimed is disclosed.

3.3 The problem to be solved by the present invention may therefore be regarded as the provision of an alternative process for the preparation of 1-naphthylethylamine

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compounds as well as enantiomers thereof.

In view of D1-D4 the solution proposed in claim 2 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT), because the claimed process is an analogy process using a different known starting ketone. Furthermore the skilled person already knows from D5-D7 that 1-naphthyl ethyl alcohol of formula (7) or (9) can be produced from the 1-acetonaphthone in high enantiomers selectivity (see especially D6, table I and D7, table 2, entry 14).

Therefore the features disclosed in D5-D7 and D1-4 would be combined by the skilled person, without exercise of any inventive skills in order to solve the problem posed.